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Case Report

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A forgotten diagnosis in the emergency department: adult-onset still's disease

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ABSTRACT

Adult-onset Still disease (AODS) is rare condition that can be the cause behind high fever,rashes and joint aches in adult patients. Being a rare condition often times it is overlooked as an improbable condition. Its prevalence is estimated to be 1 in 100,000. AODS generally presents itself in young adults, however in our case the patient was a lactating mother.Yamaguchi criteria remains as the diagnostic criteria for AODS. Our case report aims to demonstrate the diagnostic process and subsequent treatment of this rarely encountered condition.

Keywords: Fever, rash, Still's disease, arthralgia

INTRODUCTION

Adult-onset Still's disease (AOSD), first described by Bywaters in 1971, is a systemic connective tissue disease of unknown etiology. It is characterized by fever, rash, and joint finding.[1] The disease may present with high fever alone, without typical skin rashes and joint findings.[2-6] Its prevalence is estimated to be 1 in 100.000, and the disease is thought to predominantly affect young adults. However, AOSD also presents itself in bimodal age groups, with the other affected group being 46–64-year-olds alongside young adults. This report aims to describe the symptoms and laboratory and imaging workups of a patient with adult Still's disease.

CASE

A 33-year-old breastfeeding mother with no past medical history other than a C/S operation one month ago presented to the emergency department with intermittent fever, malaise, and a rash that started under the neck for the last two days. The patient's evanescent salmon-colored maculopapular rashes fluctuated in the presence of a fever. She had experienced widespread joint pain and difficulty in movement for the past 2 days. There were no prodromal or prior symptoms in the patient's medical history. She described the onset of the symptoms as an abrupt event. Vitals were within normal limits except 38°C of fever. On physical examination, the patient was conscious, oriented, and cooperative, with no neck stiffness, and the oropharynx was hyperemic. Breath sounds were normal. Her wrists and right knee were swollen and her range of motion was restricted. Leukocyte count of 12,000/µL) (normal range: 3,800-10,000/µL), neutrophil count of 9,850 /µL (normal range: 1,560-6,130/µL) and eosinophil count of 440/µL (normal range: 40-3603/µL), CRP 224 mg/L (normal range: 0-5 mg/L), procalcitonin level of 3.57 µg /L (normal range: <0.5 µg /L), ferritin level of 579 µg/L (normal range: 13-150 µg/L) was detected in the blood results. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were within normal limits, and lactate dehydrogenase (LDH) levels were 310 U/L (normal range: 135-214 U/L). Antinuclear antibody (ANA) and rheumatoid factor (RF) tests were negative. The leukocyte count was 1+ in the urine analysis. The peripheral blood smear results were negative. Brucella and viral serology tests were negative, and the blood and urine cultures yielded negative results. The tests were conducted at an inpatient clinic. No vegetation was observed on bedside echocardiography. Additional imaging revealed splenomegaly (present. The patient was evaluated using the Yamaguchi criteria with a potential diagnosis of Adult-Onset Still's disease. With the characteristic rashes, arthralgia and leukocytosis of which 80% consisted of granulocytes, three major conditions were fulfilled. The patient also had a sore throat, negative test results for both RF and ANA,

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and splenomegaly, fulfilling the three minor conditions for the Yamaguchi criteria. We also evaluated the patient using Yamaguchi exclusion criteria to clarify and confirm the potential diagnosis and to eliminate confounding conditions such as malignancy, infection, or other rheumatoid diseases. There were no prior symptoms older than two days, and the patient did not experience any weight loss or fatigue before the inception of the symptoms. This has pushed us away from a potential diagnosis of malignancy. Urine analysis and blood culture did not show positive results for potential infections. Alongside echocardiography, which showed no vegetation, these findings prompted us to search for an alternative diagnosis other than a potential infection. RF and ANA tests also had negative results, which is not a definitive exclusion criterion for other rheumatological diseases, but provided us with a direction towards the diagnosis of AOSD. After the initial treatment and evaluation, the patient was admitted to the internal medicine inpatient clinic with a preliminary diagnosis of adult-onset disease for further examination and treatment. In the internal medicine inpatient clinic, the patient was treated with anti-inflammatory therapy consisting of corticosteroids and non-steroidal anti-inflammatory drugs. Symptoms started to resolve after 48 h, and the clinical status of the patient did not deteriorate towards macrophage activation syndrome. The patient survived and was discharged from the internal medicine clinic a week after receiving a follow-up appointment.

DISCUSSION

AOSD is a rare systemic inflammatory disorder of unknown etiology. The pathogenesis of AOSD relies on the activation of innate immune cells and involves the overproduction of pro-inflammatory cytokines, such as IL-1, IL-6, and IL-18. Treatments aim to neutralize these agents by using different ranges of available drugs. However, as the complete mechanisms behind AOSD remain unclear, treatment arrangements depend on the response and clinical outcome of the individual patient. Certain triggers are suggested to be responsible for the activation of the disease, such as infections or genetic background, but none has been definitively proven.[7]

AOSD shows no pathognomonic laboratory findings. It is important to exclude infections, neoplasms, and other systemic diseases with similar clinical findings. Although different criteria have been proposed for the evaluation and diagnosis of AOSD, the Yamaguchi criteria described by Yamaguchi et al.[8] in 1992 remain the most widely used and validated.

The Yamaguchi criteria contain major and minor elements. Persistent fever (>39 °C for over a week), arthralgia, rash, and neutrophil-dominant leukocytosis (>80% neutrophils and >10x103/μL white blood cells) were described as the major elements. To meet these criteria, the patient must fulfill five major or minor elements. Minor elements included sore throat, lymphadenopathy or splenomegaly, increased serum aminotransferase or lactate dehydrogenase levels, and negative IgM rheumatoid factor and antinuclear antibodies. As mentioned previously, our patient fulfilled three major and three minor criteria. There are also exclusion criteria mentioned in the Yamaguchi criteria, which consist of infections, malignancies, and other rheumatoid diseases. We did not detect any exclusion criteria in our case.

According to literature, there are two different phenotypes of AOSD. The first phenotype is a more systemic manifestation involving fevers, rashes, and more severe symptoms. The second phenotype, however, is described as a more insidious disease with arthralgia and symptoms around joints forming the background and eventually turning into a chronic articular pattern.[9] In our case, we observed an example of the first phenotype with rashes, arthralgia, leukocytosis, and a more systematic manifestation of the disease.

In our case, the ferritin levels were significantly lower than those in most other cases (500 μg/L compared to 1000 μg/L in most cases). Ferritin has been suggested as a potential biomarker for AOSD, with ferritin levels over the normal limit having high sensitivity for AOSD diagnosis. If the ferritin levels are found to be over 5 times the normal limit, sensitivity is detected at 40% and specificity is detected at 80%.[7-10] Our patient also presented with splenomegaly, which occurs in only 30% percent of the AOSD patients.[11] This is supported by the literature as well.

The treatment for AOSD remains empirical; however, the first-line therapy for AOSD is generally initiated with the use of non-steroidal anti-inflammatory drugs (NSAID), specifically indomethacin (150–200 mg). NSAID are considered ineffective in many patients; thus, the main therapy for the first-line treatment of AOSD is considered to be corticosteroids with doses of 0,5 mg from 1 mg/kg. If this treatment proves uneffective current treatment options suggest the usage of biologic disease-modifying antirheumatic drugs (DMARD) In this purpose; Canakinumab and Anakinra are widely employed in the treatment of AOSD.[12]

CONCLUSION

AOSD is a rare systemic inflammatory disease. It is difficult to diagnose because the disease has no pathognomonic findings, presents with systemic findings, and is often confused with many other systemic diseases. The case in this report met two of the major and three minor Yamaguchi criteria. The patient was diagnosed with adult still disease in the emergency department and was transferred to an internal medicine inpatient service. This report reminds us that AOSD may be present in patients who have repeated admissions to the emergency department with fever and no obvious infectious or neoplastic pathology has been detected in their examinations and who have not received a specific diagnosis.

ETHICAL DECLARATIONS

Informed Consent

The patient signed the free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declared that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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